Congress in Leningrad in 1935. He warned us that the ties of international science would not be strong enough to prevent war, though war is "essentially a bestial method of settling difficulties, a method unworthy of the human mind with its unlimited resources." But the Congress promised new friendships and was altogether a splendid affair, a fitting tribute to its world-renowned president. He was in his 86th year, a venerable but not an aged figure. He died six months later, after a short illness.

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MYXOEDEMATOUS MADNESS

BY

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Myxoedema is one of the most important, one of the least known, and one of the most frequently missed causes of organic psychoses—important because it may respond so gratifyingly to treatment, little known because little has been written about it, often missed because the textbook description of myxoedema is not the rule but the exception.

Fourteen cases are here described, all of which had myxoedema and psychotic changes. In every one of them the diagnosis was confirmed beyond doubt. They all showed a psychosis amounting to complete "madness," ten being admitted to the mental observation wards under the Lunacy Act, one referred to the neurosurgeon for cerebral tumour, and three to general medical wards with other diagnoses. In nine of the cases there was a dramatic and complete recovery of sanity with thyroid treatment, in two there was partial improvement, one showed no change, and two patients died. The fact that in none of these cases had the diagnosis been made by the outside doctor suggests that there is need for increased awareness of myxoedema as a cause of psychoses, and, further, shows that it may be worth while discussing how myxoedema can be diagnosed so that cases may be recognized and treated early.

The average doctor is well aware that dullness and a poor memory are caused by myxoedema, but does not realize that a frank psychosis can occur. Dr. Leonard Simpson, in Price's *Medicine*, describes the condition clearly and stresses its importance, but most of the popular textbooks omit any reference to it at all, and this may account for the rarity of its recognition. Apart from medical textbooks, A. J. Cronin (1937) paints a vivid if sensational picture of a "mad myxoedema," and it was from this source that I first learned of the condition. Though Stoll (1932) described six personal cases, the fact that Zondek and Wolfsohn (1944) published one solitary case of myxoedematous psychosis in 1944 suggests again that it is regarded as a rarity. Nevertheless, the condition was clearly described, and was recognized as exceedingly common by the Committee of the Clinical Society of London (1888) appointed in 1883 to consider the subject of myxoedema. Their report says (p. 31): "Delusions and hallucinations occur in nearly half the cases, mainly where the disease is advanced. Insanity as a complication is noted in about the same proportion as delusions and hallucinations. It takes the form of acute or chronic manias, dementia, or melancholia, with a marked predominance of suspicion and self-accusation." (At the time of that report thyroid treatment was quite unknown, so doubtless many of the cases would to-day have been diagnosed and treated before mental symptoms arose.) I want to make it clear that I am not describing something new, but something old that is nowadays often forgotten.

Is there a Specific Type of Psychosis Associated with Myxoedema?

This question is fully discussed by Akelaitis (1936). The possible theories are: (1) that myxoedema produces a psychosis depending on the "pre-psychotic reaction type"; (2) that it produces a specific type of psychosis; and (3) that it produces psychoses of various types, either resembling one of the ordinary idiopathic psychoses or else typical of no special type.

Cases in the literature record a very wide variety of mental changes, and certainly in the series I have observed there has been no constant type of psychosis, though general confusion and disorientation with persecutory delusions and hallucinations, and occasional bouts of restless violence, have been common. I have made the diagnosis on the myxoedematous appearance of the patient and not on the kind of mental symptoms. No physician would attempt to diagnose lobar pneumonia or typhoid by the delirium they may produce, and likewise in myxoedema it is the disease which is the characteristic feature, not its mental manifestations.

The fact that recorded cases of myxoedema psychosis have closely resembled paranoia (Case 1 and Stoll, 1932), schizophrenia (Zondek and Wolfsohn, 1944), melancholia (Buschan, 1896), or other orthodox psychoses does suggest that the common psychoses—schizophrenia, mania, melancholia, paranoia, and so on—may turn out to be not diagnoses in themselves, but manifestations of underlying organic disease.

Does the Response to Thyroid Prove the Myxoedematous Origin of the Psychosis?

First, if the case responds it is of course no absolute proof, because almost any type of psychosis can improve spontaneously. Nevertheless, when mental symptoms that have been present in a hypothyroid patient for many months clear dramatically within a few weeks of starting thyroid it is reasonably certain that they were due to myxoedema.

Secondly, if the mental changes persist after adequate thyroid treatment, does this mean they were not myxoedematous? As Ruhberg (1936) points out: "It is necessary to determine if they are secondary to thyroid insufficiency or merely a coincident concomitant." He states dogmatically: "If the mental symptoms are part of myxoedema, improvement and relief should be obtained by establishing a normal basal metabolic rate." Akelaitis (1936), discussing cases which showed physical but not mental improvement with thyroid, also concludes: "The psychosis was a coincidence and not part of the myxoedema." Such dogmatic assumptions are unjustified. It is generally agreed that metabolic changes can produce irreversible damage—for instance, the changes of prolonged hypoglycaemia or of pellagra may fail to respond respectively to glucose or to the vitamin B complex, although they were caused by deprivations of these. Again, the belated treatment of cretinism shows that the changes in the brain cannot be reversed by thyroid.

Dr. Leonard Simpson (personal communication) records such a case in which peculiar behaviour persisted after thyroid treatment and ultimately ended in psychosis. Hence

prolonged thyroid deficiency may well cause a psychotic change which does not respond to thyroid. I believe that myxoedema, if left untreated, can produce an incurable psychosis, and I consider that those cases that have not been completely cured (Cases 1, 2, and 8) with thyroid were nevertheless initially caused by lack of thyroid, especially as two of them improved a great deal at the beginning of treatment.

I can give no certain evidence (from analysing these fourteen cases) that the longer the myxoedema is left untreated the poorer is the outlook for recovery, though this is what one would expect. It is so hard to determine when the myxoedema started that one can only guess at the answer.

Case 1

A housewife aged 55 was admitted on an authorized officer's order on Aug. 26, 1944, confused, hallucinated, and with persecutory ideas. Fourteen years previously she took her child to another hospital with a whitlow. The casualty officer, noticing that she herself looked thyrotoxic, referred her to a surgeon. Total thyroidectomy was performed. On discharge she was instructed to take thyroid, but stopped doing so after five years. She had thus been without thyroid for the nine years preceding her admission. For three years her daughters had noticed her increasing deafness, hoarseness of voice, and mental strangeness. She believed neighbours and others were plotting to harm her; she heard imaginary voices, and sometimes expressed delusions of grandeur.

On examination she was seen to be mentally retarded, apathetic, and sluggish. Occasionally she would become excited and complain of hearing voices or that the nursing staff was plotting to kill her. She was so confused and disorientated that she was unable to give an account of herself. She had the typical appearance of advanced myxoedema with gross non-pitting oedema of the whole body. She had well-marked supraclavicular pads, scanty eyebrows, thick croaking voice, and dry scaly skin. She was slow and ponderous in both body and mind. Her pulse was 65 and the blood cholesterol 362 mg. per 100 ml.; it was not possible to take the basal metabolic rate.

In addition to myxoedema she had gross elephantiasis of the left leg with scars of a previous Kondoleon operation. This elephantiasis had come on rapidly eight years previously. At the time of the operation (four years previously at another hospital) the house-surgeon, after describing the leg, records: "whole body now solid with lymphatic oedema." This suggests that she was really grossly myxoedematous at that time, but that because she had lymphatic oedema of the leg the generalized swelling was incorrectly assumed to be lymphatic oedema also.

Progress.—She was treated with 1 gr. (65 mg.) of thyroid four times daily, increasing by 1 gr. a day till she was taking 8 gr. (0.52 g.) daily. The blood cholesterol came down as follows: Aug. 29, 362 mg. per 100 ml.; Sept. 5, 354 mg.; Sept. 18, 230 mg.; Sept. 26, 158 mg. The thyroid was then reduced to 1 gr. four times daily, whereupon the cholesterol rose to 273 mg. by Oct. 13. The thyroid was again increased to 2 gr. (0.13 g.) four times daily and the cholesterol came down again; thus on Oct. 24 it was 225 mg. and on Nov. 7 163 mg. It therefore seemed that she required this large dose of 8 gr. a day, and, having had a *total* thyroidectomy, this was not surprising. During treatment her physical improvement was slow and her mental improvement disappointing. After six weeks she had lost 7 lb. (3.18 kg.) in weight and her appearance was noticeably less myxoedematous. Mentally there was an increase in alertness and sufficient decrease in disorientation and noisiness for her to be transferred from the mental observation ward to a general medical ward on Oct. 19; but she continued (though less constantly) to behave peculiarly and she had to be sent back to the observation ward on Nov. 6. Three months after admission (Nov. 28) she had lost over 14 lb. (6.35 kg.) in weight and the improvement in her appearance was more apparent, but as she did not show any further mental improvement she was transferred to Shenley Mental Hospital. Though she still thought other patients were making accusations against her and stated that she and King George VI jointly owned the hospital, there was a great improvement compared with her mental state on admission, for she could give a full account of her previous history and was far less confused.

Case 2

A housewife aged 60 was admitted on an authorized officer's order on Dec. 20, 1945, with delusions of persecution and hallucinations. For six months she had noticed that her voice was croaking and she felt cold weather badly, but she had noted no other myxoedematous symptoms—no gain in weight, falling out of hair, or deafness. During the week before admission she had an idea that her landlord was trying to poison her "because she knew all about the shootings in the back garden," she heard voices talking to her continuously, and locked herself in her room to protect herself from imaginary enemies.

On examination she was completely confused and disorientated, and showed the delusions and hallucinations described above. Her appearance was that of advanced myxoedema, with puffy face, malar flush, toad-like skin, scanty hair, and croaking nasal voice. She slept a great deal, with unusually sonorous snoring. The pulse was 60, cholesterol 374 mg. per 100 ml., basal metabolic rate −26%, blood pressure 170/90.

Progress.—She was treated with 1 gr. of thyroid thrice daily, starting on Dec. 24. She made steady improvement, both mental and physical: after a week she lost her delusions and realized that they had been absurd. After a fortnight she was rational, orientated, and almost completely clear. After three weeks she had lost 14 lb. (6.35 kg.) in weight and now slept without snoring. (This was a particularly striking feature of the case.) Her appearance was much improved and the blood cholesterol had come down from 374 to 250 mg. per 100 ml. After a month she was transferred to a general medical ward for a cataract operation. She stayed there five months because her eye was slow to clear up and there was delay over her new glasses. She behaved rationally most of the time, but occasionally complained that she was being watched. She was discharged for convalescence on June 7, 1946.

Two months later she wrote to the ward sister complaining that she was under the control of a mysterious man's voice, and on Sept. 7, three months after her discharge, she was readmitted to the mental observation wards complaining that this man's voice was talking to her all the time and controlling her actions. On readmission her blood cholesterol was 276 mg. per 100 ml. and her basal metabolic rate was −25%. She did not look frankly myxoedematous. Treatment with 2 gr. (0.13 g.) of thyroid thrice daily brought her blood cholesterol down to 150 mg. in three weeks, but there was no corresponding mental improvement, and on Nov. 15 she was certified and transferred to Shenley Mental Hospital.

Case 3

A housewife aged 50 was admitted on an authorized officer's order on Aug. 16, 1946, with delusions and hallucinations. For three months she had been getting increasingly dull mentally, gaining weight, and becoming constipated. For one week she had expressed ideas of persecution, saying that many people were plotting against her. She also believed that she was ridden with incurable diseases, and that she might infect everyone. She was continuously terrified by strange voices and strange faces.

On examination she was hallucinated, deluded, and persecuted as described above. She told the doctor estimating her basal metabolic rate that he was in danger of catching typhoid, syphilis, and cancer if he came near her. She was slow in her responses and very depressed and disorientated. Her appearance was typically myxoedematous. The "strawberry and cream" complexion was well marked (the malar flush shows

FIG. 1.—Case 3; Aug. 26, 1946.

FIG. 2.—Case 3; April 14, 1947.

well in Fig. 1, which also shows that the outer thirds of the eyebrows *can* be well developed in myxoedema) and the palpebral tissues were narrowed by compression with myxoedematous tissue. The voice was thick, grating, and nasal. Her hair was coarse but profuse, and her skin thick and scaly. The pulse was 76, cholesterol 428 mg. per 100 ml., basal metabolic rate −25%, and blood pressure 155/110.

Progress.—On Aug. 23 she was given 1 gr. of thyroid twice daily, the dose being gradually increased to 2 gr. three times a day on Sept. 12. There was a very rapid improvement in both her appearance and her mental state. Unfortunately, the first photograph (Fig. 1) was taken when she had received thyroid for three days, and shows a perceptibly less myxoedematous state than on admission. Within 10 days she was much more alert, and as well as being free from delusions and hallucinations she had insight—realizing the foolishness and absurdity of her previous ideas. Her cholesterol had come down from 428 to 253 mg. per 100 ml., but her basal metabolic rate was still −22%. When she had become clear-minded she told us that she had been in Redhill Hospital two years before, where she had been given some tablets which made her feel brighter and thinner. (Inquiries at Redhill disclosed that she had been an in-patient there from Nov. 12 to 21, 1944, suffering from myxoedema, and had rapidly improved with 2 gr. of thyroid thrice daily. After discharge, her practitioner had discontinued the treatment.) Her mental and physical improvement continued rapidly; she was discharged to the out-patient department a month after admission and continues to attend there in very good health. Fig. 2 shows her appearance on April 14, 1947.

Case 4

A housewife aged 73 was admitted on Dec. 23, 1946, as a case of "bronchitis." On admission she was quite confused, could give no coherent history at all, and was obviously grossly demented. She showed no evidence of actual delusions or hallucinations. A history was not available.

FIG. 3.—Case 4. This patient collapsed suddenly six days after admission.

On examination she was stuporous and slow, had occasional bouts of restlessness, and was grossly demented. She was flagrantly myxoedematous (Fig. 3). Her whole body was spongy with myxomatous tissue, which was especially striking around the eyes and above the clavicles, and which distended the lower lip. Her voice was thick, croaking, and nasal in character. She breathed with a thick, stertorous snorting sound. Her hair was scanty. Her colouring was of the classical pink-and-white variety. The pulse was 60 and the cholesterol 166 mg. per 100 ml. (a surprisingly low figure). She was too ill for the basal metabolic rate to be taken. The blood pressure was not recordable.

Progress.—She was given thyroid, ½ gr. (32 mg.) thrice daily, on admission, increased two days later to 1 gr. thrice daily. Five days after admission she became more restless and confused, disturbing the rest of the ward. The next day she suddenly collapsed, became cyanosed and unconscious, with bubbling respiration, and died shortly afterwards.

Post-mortem examination showed a small thyroid (13 g.) with normal macroscopic appearance, but microscopically showing marked fibrosis, atrophy of the lobules, and almost complete absence of colloid, with replacement by lymphoid tissue. The heart (480 g.) showed myocardial hypertrophy of both ventricles, with gross dilatation of the right heart. The lungs showed congestion and oedema, with some pus in the trachea and main bronchi.

Case 5

A housewife aged 72 was admitted to a medical ward on Jan. 6, 1947, having collapsed unconscious five hours before admission. She was just recovering consciousness when admitted. For two years she had been putting on weight and feeling tired, drowsy, and unusually cold. She had also noticed her hair falling out and her hearing getting worse. On the day of admission she collapsed unconscious, with snoring respiration,

FIG. 4.—Case 5; Jan. 6, 1947.

FIG. 5.—Case 5; Jan. 1, 1948.

On admission she was slow and inclined to ramble, though rational and orientated. Two days later she became completely confused, noisy, and irrational. She had no idea where she was, and repeatedly said, "I must go home and look after my son." The other patients were so much upset by her restless mutterings that she had to be transferred to the mental observation ward.

She had a typical myxoedematous appearance and colouring. The oedema of her eyelids was particularly pronounced; her left eye, blind and atrophied after an old injury, was completely occluded by myxomatous swelling, and appeared visible only after thyroid treatment. The pulse was 70, cholesterol 320 mg. per 100 ml., blood pressure 220/120. The basal metabolic rate could not be taken.

Progress.—She was started on thyroid, ¼ gr. (16 mg.) twice daily on Jan. 7, increased gradually to 2 gr. three times a day on Jan. 18. There was rapid improvement in both her mental confusion and her myxoedematous appearance (see Figs. 4 and 5). (Note how the atrophied left eye, previously walled in by oedema, has become visible as the swelling subsided.) The blood cholesterol came down from 320 to 130 mg. in a fortnight. She became mentally quite clear within a week and was transferred back to a general medical ward. After a month she was discharged perfectly clear mentally, and physically free from any signs of myxoedema. She continues to attend the out-patient department for further supplies of thyroid.

Case 6

A woman of no occupation aged 67 was admitted on an authorized officer's order on Feb. 4, 1947, demented, confused, and disorientated. Her landlady said that for three years she had been "going senile." She needed reminding about everything and took two hours to get ready to go out. Once a fine pianist, she had lost all interest in music. During the week before admission she had attacks of screaming and violence, set her nightgown on fire, and became generally quite unmanageable.

On examination she was so slow and lethargic that she would fall asleep while being interviewed; she was quite confused and out of touch with the world, and was unable to give any account of herself whatever.

Physically, she gave an immediate impression of myxoedema. She had the pink-and-white complexion; coarse, thick skin and hair; slow, deep, nasally obstructed voice; and scanty eyebrows. The pulse was 66, cholesterol 300 mg. per 100 ml., blood pressure 156/100. The basal metabolic rate could not be taken.

Progress.—On Feb. 4 she was started on ¼ gr. of thyroid three times a day, gradually increasing to 2 gr. three times a day on Feb. 24. There was a rapid improvement in both her appearance and her sanity. Within a fortnight she was fit for a general ward and within a month was discharged. Her blood cholesterol had fallen from 300 mg. per 100 ml. on admission to 125 mg. on discharge. She attends her own doctor for further supplies of thyroid, and is in good physical and mental health.

Case 7

A housewife aged 54 was admitted on an authorized officer's order on March 13, 1947, with alternating excitement and depression, and ideas of persecution. For one year she had been getting slow and dull, and losing interest in herself and the house. A marked increase in weight and coarsening of her features had been noticed by her relatives. Her sister-in-law said: "When I was in a hospital once I saw somebody with 'lack of thyroid,' and she looked just like my sister-in-law does now, so I've always thought she must have the same illness. I tried to persuade her to see a doctor, but she wouldn't go." For a week before admission she had been alternately excitable and depressed, at times behaving violently. She had told her relatives that various people were plotting to do her harm and she had accused her husband of attempting to poison her.

On examination she was depressed, confused, and persecuted. She babbled disconnected nonsense about fire-and-water vengeance and the Bible, and could not give any rational account of herself. Whenever anyone approached her bed she would cling to their hands, begging for mercy. She showed the appearance of advanced myxoedema (Fig. 6). Her face was bloated and she had a butterfly-shaped flush on the nose and

FIG. 6.—Case 7; March 13, 1947.

FIG. 7.—Case 7; April 21, 1947.

FIG. 8.—Case 7; April 6, 1949.

cheeks. Her skin was thick and rough. Her voice was thick and hoarse, with a nasally obstructed quality. The lips were noticeably thickened. The scalp hair was fine and plentiful, the eyebrows sparse. The pulse was 60, blood cholesterol 364 mg. per 100 ml., blood pressure 180/110. The basal metabolic rate was impossible to take.

Progress.—On March 14 she was given thyroid, ½ gr. three times a day, increased gradually to 2 gr. three times a day on March 20. At first there was rapid improvement in her physical appearance, with no corresponding mental change. Fig. 7 shows clearly both the depressed mental state and the striking change in facial appearance after a month's treatment. Her blood cholesterol came down from 364 to 226 mg. in three weeks. Her depression, persecutory ideas, and general unruliness continued for five weeks, and, if anything, thyroid treatment seemed to lend more vigour to her misbehaviour—she was a sore trial to everyone. Then suddenly on April 21 she became rational, cheerful, and orientated, with almost complete amnesia over her period of confusion. For a further week she had occasional bouts of weeping, after which time she remained cheerful, happy, and perfectly normal both mentally and physically (Fig. 8). She continues to attend as an out-patient, in vigorous health.

Case 8

A housewife aged 62 was admitted on an authorized officer's order on May 15, 1947, with systematized delusions. Her sister said she had always been rather simple. For one month she

FIG. 9.—Case 8; May 18, 1947.

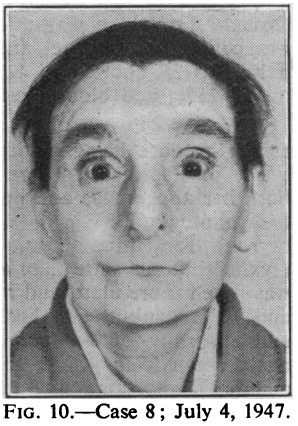

FIG. 10.—Case 8; July 4, 1947.

had become restless and deluded. She wandered round the house, packing up her belongings and saying that she was going to the seaside. She maintained solidly that she and her husband had a house at Leigh-on-Sea, and that there she must go (there was no truth in this whatever).

On examination she was quiet and co-operative, but incapable of giving a history and unwilling to submit to a basal-metabolic-rate test. She insisted that her husband was living somewhere in the hospital. Throughout her stay she persisted with the delusion that she had a house at Leigh-on-Sea. She was a shrivelled little old lady, not very myxoedematous to look at (see Fig. 9). She had wrinkled dry skin of yellowish parchment colour. There was gross alopecia. Her voice was high, with a grating, scrannel character, but was not the usual myxoedematous voice. There were no other signs. The pulse was 80 and the blood cholesterol 400 mg. per 100 ml.; the basal metabolic rate was impossible to obtain, and the blood pressure was not taken.

Progress.—She was started on thyroid, 1 gr. thrice daily, gradually increasing to 3 gr. thrice daily. There was a steady change in her appearance, as can be seen from Fig. 10. Within six weeks she looked 15 years younger. The blood cholesterol came down steadily thus: May 15, 400 mg. per 100 ml.; May 25, 349 mg.; June 4, 287 mg.; June 24, 218 mg. It was most disappointing that there was no corresponding mental improvement. She persisted in her delusions with, if anything, more conviction and vigour than before. I waited two months to see if the psychosis would clear, and then, on July 9, transferred her to Shenley Mental Hospital as a certified patient.

Case 9

A housewife aged 56 was transferred from Hillingdon Hospital on May 28, 1947, for investigation as a case of suspected cerebral tumour or subdural haematoma. She had already been diagnosed as suffering from myxoedema.

One year previously she had been admitted to Hillingdon as a possible case of Alzheimer's disease. At that time she complained of six months' chronic head pains, depression, loss of concentration, and attacks of palpitations and panic. She was said to have been a lively person and good company before the illness, but had become so dull she could not work out ordinary money problems. On that admission nothing abnormal was noted, though she was observed to have an unusually deep, husky voice. She was discharged slightly improved after three weeks.

She was readmitted to Hillingdon on April 26, 1947, suffering from right thoracic herpes zoster and mental symptoms. She was completely confused, and was comatose most of the time but occasionally restless and violent.

Physical examination revealed an appearance of myxoedema. She had a sallow thick skin, a husky deep voice, and scanty eyebrows. There were oedematous pads above both clavicles and she was very deaf. The pulse was 90, basal metabolic rate −27%, blood cholesterol 333 mg. per 100 ml., blood pressure 200/120.

She was treated with thyroid, 3 gr. daily for 14 days, reduced after three weeks to 1 gr. daily. During a bout of restlessness on May 4 she fell out of bed and sustained a large haematoma in the centre of the forehead. Because of increased mental confusion and a suggestion of early papilloedema she was transferred on May 28 to the Central Middlesex County Hospital under Mr. T. I. G. James for neurosurgical investigation.

On admission she was still mildly myxoedematous in appearance. The blood cholesterol was 272 mg. per 100 ml., the pulse 75. No abnormal neurological findings were made. The encephalogram was normal. It was therefore considered that her mental symptoms were myxoedematous. The dose of thyroid was increased to 2 gr. three times a day. She was transferred back to Hillingdon on June 16, where, with further thyroid treatment, her mental condition gradually became normal and she was discharged for convalescence on July 11.

Case 10

A housewife aged 64 was admitted to Hillingdon Hospital under Dr. C. G. Barnes on Feb. 21, 1948, as a case of "chronic heart and renal back pressure." Dr. Barnes kindly asked me to see her on Feb. 27. Her husband stated that for one year her face had been getting puffy, for six months she had swelling of the legs and difficulty in walking, and for one month she had been bedridden. A week before admission she became quite confused and delirious, and remained so until the day of admission, when she became comatose.

On examination she was semicomatose, with shallow respiration and a slow pulse. Her eyes were completely closed by oedema and could not be opened. Her face was typical of an unusually advanced degree of myxoedema, with a striking yellow skin and malar flush. She was partially bald, her eyebrows were scanty, and her eyelashes almost completely absent. The pulse was 60 and blood cholesterol 486 mg. per 100 ml.; the basal metabolic rate was impossible to obtain.

She was given 10 gr. (0.65 g.) of thyroid the same day, as Dr. Barnes feared that otherwise she would suffocate or die from bronchopneumonia.

Progress.—During the next two days she became more deeply comatose, but on the third day she became conscious and her eyes were visible. She was restless and hallucinated. She complained that "Joe the Shadow" was trying to do her harm and that people were watching her. She shouted about pictures on the ceiling and told me that she heard pianos and singing. She remained maniacal and hallucinated for over a fortnight. She was given 1 gr. of thyroid daily and her myxoedematous appearance and her mental state steadily improved. After two months she looked nearly normal and her confusion had almost gone. On April 1 the basal metabolic rate was +2% and the blood cholesterol had come down from 486 to 314 mg. per 100 ml. She was discharged home on April 1, fit and rational.

Case 11

A housewife aged 53 was admitted on Feb. 23, 1948, complaining of tiredness and undue gain in weight. Fifteen months previously she had had a cholecystectomy for gall-stones. For six months she had felt weary and had gained much weight. She complained of chronic catarrh and said her voice had become coarse and her skin rough.

On examination she was slow and rather drowsy, but appeared rational until a week later, when she showed delusions of persecution. She said she had been accused of wrongdoing by the hospital staff and believed that she had been admitted for punishment. She told me that all the other patients were whispering to each other, saying unpleasant things about her. She had to be transferred to the mental observation ward on March 8, as her paranoid ideas were getting worse.

Physically she had the typical appearance of fully developed myxoedema. Her features were swollen, the normal facial creases being ironed out by the swelling. Her face was a waxy yellow colour. Her eyebrows were scanty, her skin dry, her speech thick and indicative of nasal obstruction. Her

FIG. 11.—Case 11; Feb. 24, 1948.

FIG. 12.—Case 11; June 14, 1948.

blood cholesterol was higher than that of other cases in this series—610 mg. per 100 ml. The palms of her hands had yellow bands 0.25 cm. wide, corresponding to the creases. These were cholesterol deposits, the same colour as the xanthelasma of hypercholesterolaemia, and they steadily faded during the next two months as the blood cholesterol fell with treatment. (The high blood cholesterol might also have contributed to the gall-stones from which she had suffered.) The pulse was 75 and the basal metabolic rate −8%; the blood pressure was 155/90.

Progress.—She was given thyroid, 1 gr. three times a day, on Feb. 27, increasing gradually to 2 gr. four times daily on March 19. At first her mental symptoms grew worse, while her appearance improved. By March 11 she had some insight into her previous irrationality, and by March 13 she was mentally normal, remaining so until her discharge to the outpatient department on March 25. Figs. 11 and 12 show the striking changes in her face.

Case 12

This patient was a physician aged 33. During a lecture on myxoedema to some doctors taking a membership course in 1946 I described the mental changes which I had so often encountered, and mentioned that ideas of persecution were common. At the end of the lecture the patient came up to me and explained that he was a known case of myxoedema, and gave the following history.

In 1941, while with the Army in West Africa, he felt tired, dull, and slow. At the same time he developed ideas of persecution. These symptoms continued unchanged until February, 1942, when he was diagnosed as a definite case of myxoedema and ordered thyroid, 3 gr. daily. The persecutional ideas disappeared completely in a short time and he felt a

striking improvement in his feeling of well-being. In 1945, while in Italy, he began to wonder if it was really necessary to go on taking thyroid, so he stopped. The mental symptoms crept insidiously back and there was a falling off in his general efficiency. Eventually he found himself unwilling to go into the mess with his fellow officers because he believed they were talking about him, criticizing him, and plotting against him in some way. He resumed thyroid treatment again, and his persecutional ideas once more disappeared rapidly. Since that time he has continued to take thyroid in various doses, at present being stabilized on 6 gr. daily and remaining mentally and physically quite well.

When I saw him his appearance seemed normal (I did not examine him professionally), but he had some malar flush and his voice was a little lower and slower than the average. He had not previously mentioned his mental symptoms to anyone lest they indicated a true psychotic tendency, but on learning that they were merely a part of his hypothyroid symptoms he was much relieved and quite pleased to admit them. He has very kindly agreed to my publishing these details about his case.

Case 13

A housewife aged 62 was admitted on March 18, 1949, on an authorized officer's order, suffering from confusion and dementia. Her husband said that for about four years she had been increasingly slow in mind and body. She often complained of coldness and deafness, and became very forgetful. She "snored something awful." A week before admission she became unable to walk. Her voice was so thick no one could understand her. She stared blankly about her and seemed unaware of what was going on.

On examination she was mentally in a state of hibernation, and an unintelligible croaking monosyllable was the only reply to questioning. Her mind seemed to have stopped functioning rather than to have become disordered.

Physically she was the grossest case of myxoedema in the series. Her face was bloated and misshapen, with great wine-coloured patches on a dusky yellow background. She was dirty, unkempt, and partially bald. Her skin was as cold and rough as a lizard's. Her pulse was 48, temperature 97° F. (36.1° C.), respirations 16.

FIG. 13.—Case 13. This patient died on the day after admission.

Progress.—She died early the next morning before any investigations had been done, so the cholesterol value, the basal metabolic rate, and the blood pressure were not known. A coroner's inquest reported death from acute heart failure due to myxoedema. The thyroid was completely replaced by white fibrous tissue, but was otherwise normal in size and shape. The heart was dilated and hypertrophied, and there was a pericardial effusion.

Case 14

A housewife aged 53 was admitted on an authorized officer's order on March 29, 1949, suffering from hallucinations and delusions of persecution. For three months she had complained that she was being persecuted by the people in the flat above her. She tried to persuade her husband that they were spying upon her down a ventilator pipe. She heard voices saying unpleasant things to her, particularly at night. She also began to snore excessively, and because of this she went to the out-patient E.N.T. department of a large voluntary hospital. Her delusions and hallucinations were so flagrant, however, that she was immediately referred to the psychiatric department. The senior psychiatrist then referred her to the authorizing officer as a case of paranoid psychosis.

When deliberately questioned she admitted that for two years her hair had been coming out, her voice had been getting deeper, and her skin had become dry. She said she felt so cold and sleepy she wanted to curl up and go into a long, long sleep.

On examination she was found to be persecuted, deluded, and hallucinated, and she complained of the voices pestering her continually. She was typically though not grossly myxoedematous. The skin of her face was yellow with a malar flush, the palpebral fissures were narrow, and the eyebrows scanty. Her voice was thick and croaking. Her pulse was 68, cholesterol 250 mg. per 100 ml., blood pressure 130/90. The basal metabolic rate was impossible to take (she thought she was being gassed).

FIG. 14.—Case 14; March 31, 1949.

FIG. 15.—Case 14; May 25, 1949.

Progress.—She was started on thyroid, ½ gr. thrice daily, increased five days later to 1 gr. thrice daily. Within a fortnight there was an obvious facial change and she began to have insight into her hallucinations—admitting they were not real voices though she still heard them. After three weeks the cholesterol had come down from 250 to 120 mg., the hallucinations had stopped, and she said, "I feel different, I see things different, and my husband says I look younger. I talk different; I've lost that deep tone and seem to speak lighter." She was discharged a month after admission and continues to attend as an out-patient in normal physical and mental health. Soon after discharge, when she went to her grocer he said to her: "Are you a relation of the Mrs. —— who used to come in here and went to hospital?" He had completely failed to recognize her.

Discussion

It is hoped that publication of these fourteen case reports may call attention to the very important fact that myxoedema causes psychosis. If one observer can encounter this number in four years it must mean that there are many others. Possibly there are many cases in mental hospitals which have not been diagnosed. If the diagnosis is borne in mind by psychiatrists a number of otherwise hopeless psychoses may be cured, and the awareness of an organic cause for one psychosis may lead to the discovery of physical causes for others which are at present dismissed as of psychological or idiopathic origin.

How to Diagnose Myxoedema

As this paper has stressed the importance of early diagnosis and treatment of myxoedema, it seems logical to summarize the methods by which a diagnosis can be made, especially as these case records show that in no instance was the diagnosis made before the patient came to hospital.

The history gives little help in making a diagnosis, though it greatly helps in confirming it once the condition is suspected. That is because the symptoms are admitted rather than complained of; they are dismissed by the patient as minor nuisances rather than exhibited as major complaints, and are therefore usually elicited only when the appropriate questions are asked. The mental slowness of the illness itself smothers self-criticism, and so changes may pass unnoticed by the patient while friends and relations observe them. In fact, you get no history of myxoedema if you are not thinking of myxoedema when you take that history.

The following symptoms are common: general tiredness, gain in weight, vague aching pains in the legs, poor memory, constipation, deafness, falling out of hair, dry skin, always feeling cold. All these symptoms commonly occur in non-myxoedematous people and not one of them is constant in myxoedema. Change in the facial appearance, alteration in the voice, and snoring are usually noticed by relatives rather than by the patient.

The only way to ascertain what a case of myxoedema looks like is to see one. No amount of description can convey the unmistakable impression of a well-developed case. Photographs are more helpful than words, but give no idea of the characteristic colouring and voice. Here is a description of an advanced case.

Nearly all cases occur in women. The features look bloated and the normal contours of the face are smoothed away, just as the wrinkles of a balloon disappear when it is blown out. Oedema collects in the lips, broadening them, and around the eyes, forming little bags of flesh beneath them. When, after treatment, the swelling round the eyes subsides there is sometimes revealed a slight exophthalmos, possibly due to the anterior pituitary's efforts to flog an inactive thyroid. The colour is yellowish and waxy, with a contrasting burgundy-coloured flush over the malar bones. The hair is dry and scanty, the receding hair margin leaves a wide forehead, and there may be partial baldness. The eyebrows are sparse, and sometimes the lashes too. The classical loss of hair over the outer third of the eyebrows is an unreliable sign, because so many normal people show this deficiency.

The voice is slow and fumbling from the clumsy thickness of the lips and tongue, and the oedematous infiltration of the nasal passages gives it a characteristic nasal quality. It is impossible to imprison the sound in words, but the impression is that of a bad gramophone record of a drowsy, slightly intoxicated person with a bad cold and a plum in the mouth. Snoring (Morehead, 1936), already mentioned as a symptom, may be of arresting intensity, and it is odd that in a discussion on snoring at the Royal Society of Medicine no mention was made of myxoedema as one of its causes.

The description here given is that of an unusually obvious case. The recognition of an early or a mild case is harder but is more satisfying than recognizing the self-evident one. Mild cases are probably often missed because the textbook illustrations always picture an unusually gross case and not the moderate cases which are more often encountered. Mistakes are also made through expecting every sign to be present, whereas the average case lacks at least one of the classical features of the illness; for example, Case 3 had luxuriant eyebrows (see Fig. 1), Case 4 had a low blood cholesterol, Case 8 had no puffiness of the face (see Fig. 9), Case 9 had a raised pulse, and Case 11 had a normal basal metabolic rate.

Confirmatory Tests

Photographic Test.—I consider there is only one infallible confirmatory test for myxoedema. Take a good photograph; then give thyroid for a month or more and take another photograph. The change between the two photographs is a clear confirmation of the diagnosis. In many cases where I have not been certain of the diagnosis the change recorded by photographs has been the only unequivocal proof of the answer. Look at the picture of Case 8 (Fig. 9), which might well be that of just an elderly bald lady: the change of face makes the diagnosis certain, especially coupled with the changes in cholesterol. See also Cases A and B—two other examples of "non-obvious" myxoedema confirmed by photographic changes (Figs. 16, 17, 18, 19, and 20). These cases are not included in the series, because they had no psychosis: and here I would like to stress that only a proportion of myxoedema cases have psychotic changes, and that these remarks on the diagnosis of myxoedema apply to all cases, with or without mental symptoms.

FIG. 16.—Case A; May 20, 1947.

FIG. 17.—Case A; July 2, 1947.

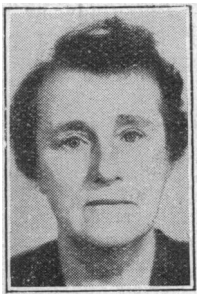

FIG. 18.—Case A; Nov. 19, 1947.

FIG. 19.—Case B; Jan. 13, 1948.

FIG. 20.—Case B; May 10, 1948.

Blood Cholesterol.—This is nearly always raised, and, furthermore, descends with thyroid treatment. In ten of these cases the initial blood cholesterol was 300 mg. or more per 100 ml., and it usually descended by over 100 mg. per 100 ml. after thyroid treatment. Blood cholesterol estimations are, after photographs, the best confirmatory tests.

Basal Metabolic Rate.—From experience with many other cases besides these I have found the basal metabolic rate of little help in diagnosing myxoedema. It is a test which is accepted when it agrees with the physician and disregarded when it does not. I have seen many cases of myxoedema with normal or raised B.M.R. Further, the presence of mental change or respiratory obstruction may prevent the estimation being done. In only four of the cases described above was the basal metabolic rate taken—Case 2 −26%, Case 3 −25%, Case 9 −27%, Case 11 −8%.

Pulse Rate.—The classical bradycardia of the textbook is not common. In four cases the pulse was over 70 and in only two instances was it below 60.

Blood Pressure.—In six of these cases there was hypertension (either a systolic pressure above 170 mm. Hg or a diastolic pressure above 100 mm. Hg).

Summary

Myxoedema is a much commoner cause of psychosis than is usually believed. Treatment with thyroid usually cures the psychosis dramatically. Fourteen cases are described—nine recovered completely, two recovered partially, one showed no change, and two were fatal. There is no specific psychosis, but paranoid ideas are common. A description of myxoedema is given and methods of diagnosing it are reviewed. Photographs before and after thyroid treatment give the best confirmation of the diagnosis.

I want to thank the visiting doctors and magistrates who left cases uncertified so that I could keep them for thyroid treatment rather than transfer them to a mental hospital. Also I must thank Miss Buckle and Mr. Booker for their excellent photographs. I am indebted to Dr. Barnes, of Hillingdon, for Case 10, to Mr. Iltydd James for Case 9, and to Dr. Pagel for the necropsy on Case 4. Dr. Leonard Simpson has given advice and criticism.

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OPTIMAL METHODS IN THE TREATMENT OF OPHTHALMIA NEONATORUM

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The relative value of sulphanilamide, sulphapyridine, sulphamezathine, sulphathiazole, and sulphadiazine in the treatment of ophthalmia neonatorum has been discussed in a previous study (Sorsby, 1945). It was pointed out that, with the dose of 0.25 g. on admission and 0.125 g. four-hourly day and night until 48 hours after clinical cure, the results obtained by different sulphonamides were essentially the same, and that sulphanilamide itself and sulphapyridine were less desirable than sulphamezathine and sulphathiazole and sulphadiazine, as they tended to give toxic symptoms rather more frequently.

Sulphamezathine seemed to be at least as satisfactory as sulphathiazole and sulphadiazine, but, like the other drugs, still gave a residue of about 15% of cases that responded either poorly or showed relapse. In a series of 84 cases treated with sulphamezathine a clinical cure was obtained within one to three days in 39.3%, 44% required four to eight days' treatment, whilst 16.7% showed an unsatisfactory response or a relapse.

The different modes of using penicillin were found to give a high rate of adequate results only when penicillin locally was applied in high concentration and at frequent intervals (Sorsby, 1947). In a series of 104 cases treated initially at intervals of one minute for half an hour (with drops in a concentration of 2,500 units per ml. in 71 cases, and a concentration of 10,000 units per ml. in 33 cases) the average total time of treatment was 38 hours. This, however, applied to only 77 of the 104 cases, while 27 showed a poor response or relapse. Likewise there were six unsatisfactory results in a total of 39 cases treated by systemic injections (800,000 units: four injections of 200,000 units each at four-hourly intervals).

Taking the whole series of 333 cases treated with sulphonamides and 143 cases treated intensively with penicillin, the percentage of failures—assessed by poor response or relapse—was considerable in both series: 16.3% with sulphonamides and 23.1% with penicillin. It was pointed out, however, that unsatisfactory response is to be understood in a relative sense only. In not a single instance was the response so poor as to cause anxiety for the state of the eye, and some of the cases classified as relapses were almost certainly cases of reinfection rather than relapse. The present study, covering 151 cases, was undertaken to determine whether better results could be obtained, particularly from the sulphonamides, by more intensive use of the agents employed.

A Series of 151 Cases

Table I sets out the 151 cases studied, classified according to causal organism and severity of the affection in relation to mode of treatment. It will be seen that *Staphylococcus albus* was responsible for the largest number of cases (33), *Staphylococcus aureus* for 22, various bacilli, including diphtheroids, for 21, and the gonococcus for 14 cases. There were 31 cases completely negative, showing neither organism nor inclusion bodies, whilst 18 cases showed no organisms but had inclusion bodies. In addition, inclusion bodies were seen in combination with causal organisms in 25 cases. The total incidence of inclusion bodies in this series was therefore 43. Of the whole series 48 cases were mild, 78 moderate, and 25 severe. The different grades of severity seemed to be fairly evenly distributed over the whole range of causal organisms. Several modes of treatment were tried out in this series.

Therapeutic Results

1. *Systemic Penicillin Therapy (30 Cases).*—In all 30 cases were treated by penicillin systemically. Four received 800,000 units of penicillin exclusively by mouth—200,000 units initially with a second dose one and a half to three hours later, and two further doses at three-hourly intervals. The response was slow and incomplete, and all four cases relapsed. This method was not tried further. Twenty-six cases received an initial intramuscular injection of 200,000 units, followed by the same dose orally one and a half to three hours later, and subsequently by two further doses by mouth at three-hourly intervals. All the 26 cases recovered, but 11 relapsed. As the method was obviously inferior to treatment by four intramuscular injections it was discontinued.

2. *Treatment by Oral Sulphamezathine with an Initial Dose of 0.5 g. and a Maintenance Dose of 0.25 g. at Six-hourly Intervals (57 Cases).*—In the previously reported series of 84 cases treated by sulphamezathine the initial dose was half that in the present series and the maintenance dose also half, but given at four-hourly instead of six-hourly intervals. The total dose of sulphamezathine was therefore increased on the first day from 0.875 g. to 1.25 g., and on subsequent days from 0.75 g. to 1 g. Table II sets out the comparative results in the two series. It will be seen